REMARKS

This Amendment is submitted in response to the final Office Action mailed on March 25, 2008. A petition for a one month extension of time is submitted herewith. The Director is authorized to charge $120.00 for the petition for extension of time and any additional fees which may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 112843-44 on the account statement.

Claims 1, 3-11, 13-16 and 18-19 are pending in this application. Claims 2, 17 and 23-25 were previously canceled without prejudice or disclaimer. In the Office Action, Claim 19 is rejected under 35 U.S.C. §112, second paragraph and Claims 1, 3-11 and 13-25 are rejected under 35 U.S.C. §103. In response Claim 19 has been amended. The amendment does not add new matter. In view of the amendments and/or for the response set forth below, Applicants respectfully submit that the rejections should be withdrawn.

In the Office Action, Claim 19 is rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Patent Office asserts that the claim recites the step of "synthesizing" as a step in a method for "producing" and that since "synthesizing" allegedly means "producing," the claim is unclear. See, Office Action, page 2, lines 15-18. In response, Claim 19 has been amended to recite, in part, wherein the naturally occurring precursor is synthesized. The amendment does not add new matter. The amendment is supported in the specification at, for example, page 5, line 29-page 6, line 1. The specification states that an aspect of the invention provides "a method of production of a nutritional or therapeutic composition for oral administration which comprises the steps of identifying, purifying or synthesizing a naturally occurring precursor that is metabolized to a compound having ananadamide activity." See, specification, page 5, line 29-page 6, line 1. As such, and in view of the current amendments to Claim 19, Applicants respectfully submit that the skilled artisan would immediately appreciate that the naturally occurring precursor may be either identified and purified or identified and synthesized before it is metabolized.

Moreover, "synthesize" is defined in the chemical sense as "to combine (constituent elements) into a single or unified entity." See, www.dictionary.com, definition of "synthesize." Therefore the skilled artisan would appreciate that certain constituent elements may be combined

to form, or synthesize, the naturally occurring precursor prior to metabolization. Based on at least these noted reasons, Applicants believe that Claim 19 fully complies with the requirements of 35 U.S.C. §112, second paragraph.

Accordingly, Applicants respectfully request that the rejection of Claim 19 under 35 U.S.C. §112, second paragraph, be withdrawn.

In the Office Action, Claims 1, 3-11 and 13 are rejected under 35 U.S.C. §103(a) as being unpatentable over the publication to Di Marzo ("*Di Marzo*") in view of U.S. Patent No. 6,552,031 to Burch et al. ("*Burch*"). Claims 14-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Di Marzo* in view of *Burch* and further in view of WO94/28913 to Kyle et al. ("*Kyle*"). In view of the amendments and/or for at least the reasons set forth below, Applicants respectfully submit that the cited references are deficient with respect to the present claims.

Independent Claims 1 and 14-16 recite, in part, a composition for oral administration, comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament. The combination of the naturally occurring precursor and a typical steroid or non-steroidal anti-inflammatory drug (NSAID) provides the advantage that synergy occurs since the combination has the ability to diminish inflammatory via different pathways. In contrast, Applicants respectfully submit that there exists no reason why the skilled artisan would combine the cited references to arrive at the present claims.

Applicants respectfully submit that there exists no reason why the skilled artisan would combine *Di Marzo* and *Burch* to arrive at the present claims. For example, because the Patent Office admits that *Di Marzo* does not disclose a combination of an anandamide precursor and an NSAID, the Patent Office cites *Burch* to cure the deficiencies of *Di Marzo*. The Patent Office alleges that *Burch* teaches the combination of oxycodone and rofecoxib, and maintains that it would be "a good motivation to the skilled artisan to replace oxycodone with anandamide as anandamide derivatives and precursors do not have the addictive characteristics of oxycodone." See, Office Action, page 5, lines 7-14. However, Applicants respectfully submit that, in contrast to the Patent Office's assertion, the skilled artisan would have no reason to replace oxycodone with anandamide to arrive at the present claims.

Opiod analgetics, such as oxycodone, may be deployed as a substitute for heroin or morphine, and can results in similar negative side-effects. For example, opiod analgetics can be extremely addictive to the user and can result in adverse reactions including miosis, perspiration, dysphoria, sedation, pururitus, obstipation, respiratory depression, orthostatic hypotention, hallucinations, hyperalgesia, delirium, induction of tolerance etc. Opiod analgetics may also cause side effects that include severe nausea, which, in fact, is known to be treated by the use of cannabinoids or cannabimimetic substances. Oxycodone, in particular, is a controlled substance in the United States both as a single agent and in combination with products containing paracetamol, or ibuprofen or aspirin (NSAIDs).

In contrast, the use of an anandamide, a naturally occurring neutransmitter found in the human body, in conjunction with NSAID's provides the synergistic advantage of the combination without, or with fewer, detrimental side effects than certain drugs, including opiod analgetics. However, opiod analgetics and antimimetics (anandamide) are pharmaceutically different effective groups characterized by different mechanisms of action. The two systems not only bring about different side effects both in terms of quality and quantity, as discussed above, but also utilize different ligands and receptors in their respective mechanisms of action. In this regard, Applicants respectfully submit that if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). This certainly applies here where the opiod analgetics and antimimetics (anandamide) are pharmaceutically different effective groups characterized by different mechanisms of action and utilize different ligands and receptors in their respective mechanisms of action.

Accordingly, and in contrast to the Patent Office's repeated assertions, Applicants respectfully submit that the skilled artisan would have no reason to replace oxycodone with anandamide to arrive at the present claims.

Moreover, Applicants also respectfully submit that each reference must be considered as a whole and those portions teaching against or away from each other and/or the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). "A prior art reference may be considered to teach away when a person of

ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant." *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

In its attempt to arrive at the present claims by combining the cited references, the Patent Office has ignored significant portions of each reference that teach away from the combination. For example, *Burch* specifically teaches away from the claimed subject matter when *Burch* teaches that a COX-2 inhibitor (such as rofecoxib) "would have advantages over NSAID'S." See, *Burch*, col. 3, lines 58-60. Applicants respectfully submit that this disclosure of *Burch* would actually lead the skilled artisan in a direction divergent from the path that was taken by Applicants in the present disclosure. *In re Haruna*, 249 F.3d 1327 (Fed. Cir. 2001). See, also, MPEP 1504.03.

Further, the Patent Office has improperly applied hindsight reasoning by attempting to selectively piece together teachings of each of the references in an attempt to recreate what the claimed invention discloses. In fact, in the instant situation, the prior art provides no teaching or suggestion of the desirability of the modification. Specifically, *Burch* provides no incentive to use any pharmacological system other than the opiod system. The fact that the prior art *may* be modified in the manner suggested by the Patent Office does not make the modification obvious. As a result, one having ordinary skill in the art would have no reason to combine the cited references to arrive at the present claims.

Accordingly, Applicants respectfully submit that the skilled artisan would have no reason to combine the cited references to arrive at Claims 1, 3-11 and 13.

With respect to Claims 14-25, Applicants respectfully submit that, for many of the same reasons presented above, the combination of *Di Marzo* in view of *Burch* and in further view of *Kyle* is also improper. Specifically, *Kyle* fails to remedy the deficiencies of *Di Marzo* in view of *Burch*. For example, *Kyle* is entirely directed toward methods and pharmaceutical compositions for treating neurological disorders, wherein the compositions include arachidonic acid, docosahexanoic acid or a combination of both. See, *Kyle*, Abstract. *Kyle* provides no incentive to combine the arachidonic acid or docosahexanoic acids with a steroidal or non-steroidal anti-inflammatory drug (NSAID) to arrive at the present claims.

Moreover, Applicants respectfully submit that simply because *Kyle* is directed, in part, toward the treatment of a neurological disorder using arachidonic acid, this does not make the combination with *Di Marzo* and *Burch* proper. In fact, what the Patent Office has done here is to apply hindsight reasoning by attempting to selectively piece together teachings of each of the references in an attempt to recreate what the claimed invention discloses. Applicants respectfully submit that if it is proper for the Patent Office to combine any number of references to arrive at the present claims simply because each reference suggests an element of the present claims, then every invention would effectively be rendered obvious. Instead, the skilled artisan must have a reason to combine the cited references to arrive at the present claims. Applicants respectfully submit that such a reason is not present in the instant case.

For at least the reasons discussed above, the combinations of *Di Marzo* in view of *Burch*, and *Di Marzo* in view of *Burch* and in further view of *Kyle* fail to render the claimed subject matter obvious.

Accordingly, Applicants respectfully request that the obviousness rejection with respect to Claims 1, 3-11 and 13-25 be reconsidered and the rejection be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims which could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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